



PROBLEM 2

[SUPPL Problem 2 # 1]

Arabic compound numbers in TAPSOC,
Roman numerals in Supplementary material

In Perspective

The 2-oxo-indole nucleus of target **2** is the core of a family of natural alkaloids. Of particular interest among these compounds are those with a quaternary C³ carbon forming part of a spirocyclic motif, from relatively simple substances such as coerulescine **3** to more elaborate structures like chitosenine **I**, both sustaining a spyrotetrahydropyrrolidine unit pivoting on C³.

As these heterocycles possess a variety of potent biological activities, the synthesis of any oxindol with a quaternary C³ and ancillary functional groups for further construction, as the reaction of Scheme 2.1 illustrates, is an attractive contribution to this field [1].

For the above reasons, authors designed this reaction to produce oxindoles with two substituents on C³ starting with a rather simple N-alkyl aniline. At this level no efforts were advanced to obtain an enantiomerically pure target **2**. Rather, authors pursued to synthesize horsfiline (**II**) and eventually spyrotripostatin (**IV**) (Figure SP2.1).

Alkaloid **II** was isolated from *Horsfieldia superba*, a Malaysian medicinal and hallucinogenic plant [2], whereas **III** was obtained from an entirely different organism, the fungus *Aspergillus fumigatus* [3], a common inhabitant of compost heaps.

If anything of biological relevance can be said about compound **III** and synthetic homologs created later is its potent effect in the inhibition of the division cycle of mammalian cells [4], a particularly interesting property of anti cancer pharmaceuticals.

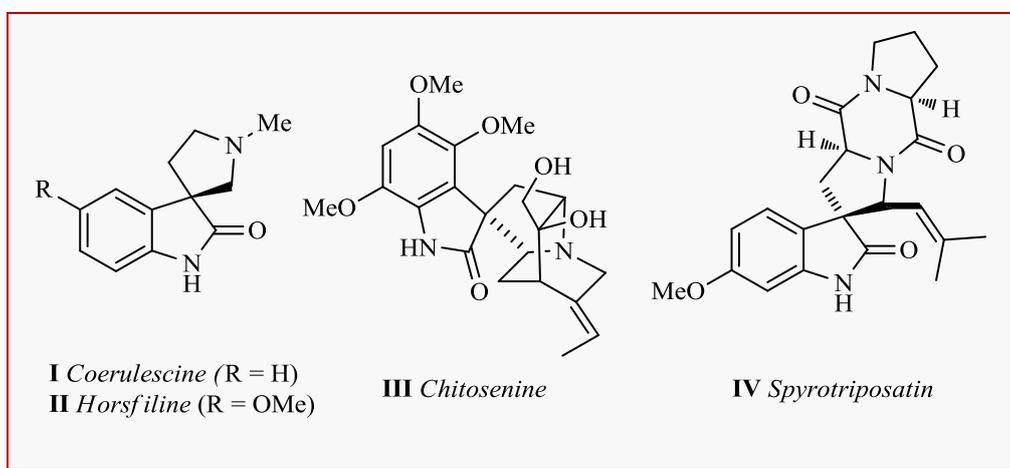


FIGURE SP2.1

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- [1] Synthetic routes to spirooxindoles with a pyrrolidine unit have been reviewed: Galliford CV, Scheidt KA. *Angew. Chem. Int. Ed.* 2007;46:8748-8758. DOI: 10.1002/anie.200701342.
- [2] Jossang A, Jossang P, Hadi HA, Sevenet V, Bodo B. *J. Org. Chem.* 1991;56:6527-6530. DOI: 10.1021/jo00023a016.
- [3] Cui CB, Kakeya H, Osada H. *Tetrahedron* 1996;39:12651-12666. DOI: 1.1016/0040-4020(96)00737-5.